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BOTANICAL GAZETTE

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THE THEORY OF RESPIRATION.^o

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I ASK you to consider with me a topic which is of fundamental interest to physiologists, whether they concern themselves primarily with animals or with plants. I take it the basal identity of the living matter in all organisms and of its metabolism needs neither demonstration nor emphasis at my hands. Nor do I need to lay stress upon the importance of respiration as one of these metabolic phenomena, since it has been recognized from the earliest period as indispensable to life. The phlogiston theory of the composition of the atmosphere had scarcely disappeared below the scientific horizon, before the fact was discovered that there occur, in animals and in plants alike, an intake of oxygen and an output of carbon dioxide which are intimately related to their existence. This became obvious to man, of course, in his own experience, a very superficial study of the composition of the air inspired and expired from the lungs showing that it had lost oxygen and gained CO₂. This much of respiration was early recognized to occur also with the larger animals, and a few years later like observations were made upon plants by PRIESTLEY, and more accurately by LAVOISIER and INGENHOUS. Even this knowledge of respiration was not possible before PRIESTLEY'S discovery of oxygen in 1774, and the very remarkable revolution in chemistry that followed in the closing years of the eighteenth century. Yet this disappearance of oxygen and formation of carbon dioxide are only the external indication of respiration, as has been long recognized.

^o Address of the retiring president before the Botanical Society of America, Philadelphia meeting, December 28, 1904. Published also in *Science*.

RESPIRATION IN ANIMALS.

Upon undertaking special consideration of this topic, I found it needful to examine the recent literature of respiration in animals, the aspect of the general subject with which I felt myself least familiar. I found, to my very great surprise, that animal physiologists have concerned themselves very little with the essential problems of respiration. They seem to have been diverted to the study of the mechanism of gas movements in the higher animals. The lungs, with their intricate structure of lobes, lobules, atria, and air "cells;" the box in which the lungs are located, with its complex muscular mechanism, and the very complicated mechanism of innervation for the voluntary and involuntary movements which it executes; the blood, and the physico-chemical relation of the gases that enter and leave it in the lungs, of those that come into it from the tissues, and of those it gives up to the tissues—these are the topics that one finds exploited at length when he turns to the text-books. I diligently examined the most modern and most thorough text-books on animal physiology; such books as FOSTER'S *Physiology*; STEWART'S *Manual of Physiology*; the *American Text-book of Physiology*; and SCHAEFER'S *Text-book of Physiology*; but in them I found no treatment whatever, indeed no mention whatever, of the real problems of respiration, that is, of what is happening in the tissues—the processes of which these external phenomena are the sign. Yet this much-studied respiratory mechanism, which is so striking in the higher animals, is entirely wanting in the lower animals and in plants.

Not finding even a clue to the literature in the text-books, it was only after much search that I was able to discover that anything at all had been done; and it is so little that it is almost a negligible quantity. There is an obvious reason for this, beside mere interest in the more striking phenomena. I am intending, however, neither arraignment nor excuse, but a bare statement of what were to me rather surprising facts.

RESPIRATION IN PLANTS.

The knowledge of respiration in plants began about the same time—the close of the eighteenth century—and advanced rapidly

on account of the notable revolution in chemistry which took place about this time. INGENHOUSS, the Dutch naturalist, really ascertained and published in 1779 the chief external facts of respiration; at least he was able to state them essentially as they were known for twenty-five years after his time. In 1804, DESAUSSURE showed that growth is dependent on respiration; that respiration is more active in growing parts than elsewhere; that it is the cause of the loss of weight to which plants are constantly subject; and later, that the heat set free in flowers is related to the absorption of oxygen. Not until 1833 was respiration treated comprehensively, when DUTROCHET expounded the subject, comparing the respiration of animal and plant, and showing it to be fundamentally alike in both.

Now at this point there began two remarkable misconceptions. One was the confusion that arose between respiration and the manufacture of carbohydrates, which DUTROCHET called "diurnal respiration." Of that I shall not speak, save to say that the great weight of LIEBIG's authority made this error persist for half a century.

RESPIRATION AND COMBUSTION.

The other misconception was engendered by the comparison of respiration to combustion. It had been observed by LAVOISIER that the heat of the animal body was dependent upon respiration; the heat of the plant body was shown by DESAUSSURE to be related to a disappearance of oxygen; combustion consumes oxygen and produces heat; therefore, respiration is a sort of combustion. So the argument ran.

It is quite impossible to overestimate the influence that this conception has had on the study of respiration. The mischief it has wrought depends chiefly, perhaps wholly, upon a misconception of the actual mechanism of combustion, a process that has ever been the *bête noire* of chemistry, as the history of the "phlogiston" theory well shows. To our changed conceptions of combustion I shall return later.

The idea of combustion, however, which dominated the argument I have cited, was that oxygen combined with carbon to form CO_2 and with hydrogen to form H_2O . It was most natural, therefore, to conceive that the food taken up by the organism stood to it in

the same relation as does fuel to the engine, and that what happens is an actual oxidation of the food immediately and directly; in fact, a process precisely parallel to the burning of the same food outside the body.

One evident outcome of that idea is the current classification of foods into plastic and dynamogenous—those which are useful in building up the body, and those that are useful in producing heat within the body; into “fattening foods” and “heat-producing” foods. You are doubtless familiar with these phrases.

But if foods are “burned” in the body, it must be important to know how much oxygen enters it, and how much carbon dioxid and water leave it, so as to discern the ratio which exists between them. Plainly a basis for this must be a comparison of the differences between the combustion of foods outside the body and their “combustion” within the body. Yet, strangely, this has not been made until recently. Without giving the full tables, let me show the results arrived at by two observers, regarding two of the most common plant foods, glucose and tartaric acid. These observers assume, you will notice, that the processes are comparable. The results are stated as ratios of $\frac{\text{CO}_2}{\text{O}_2}$.

Food	By COM- BUSTION	By RESPIRATION	
		Diakonow	Purjewicz
Glucose - - - - -	$\frac{100}{100}$	$\frac{130}{100}$	$\frac{95}{100}$
Tartaric acid - - - -	$\frac{160}{100}$	$\frac{290}{100}$	$\frac{162}{100}$

DIAKONOW's whole series shows that in combustion the carbon dioxid was always less than in respiration; PURJEWICZ found (with the exception of tartaric acid, and even there the difference between his results and DIAKONOW's is in the same direction) that it was always greater, his results being absolutely different in significance from DIAKONOW's. And this is a good type of the results to be found in examining the literature! I am not now concerned in determining which set of results is correct, inasmuch as I believe

both are valueless, since on the assumption upon which they are based neither can be interpreted.

RESPIRATORY RATIO.

Long before this sort of comparison was made, however, a voluminous literature arose which was concerned only with the ratio between the carbon dioxid given off and the oxygen consumed, and how this ratio was influenced by temperature, by light, by this kind of food or that, by mere hunger, or by starvation. This ratio, the so-called respiratory ratio or respiratory quotient, the plant physiologists really inherited from the animal physiologists, by whom it was devised with reference to the gaseous exchange that occurs in the lungs. This respiratory ratio has proved a veritable will-o'-the-wisp, leading investigators into a bog where their labors and their thinking were alike futile. For as a sign of what is going on within, the respiratory quotient is absolutely valueless, however interesting the facts in themselves may be. I could cite an indefinite number of investigations to indicate this. I select a few cases.

As long ago as 1885, RUBNER showed¹ that the respiratory ratio varied in resting muscles at different temperatures.

At 8.4°	-	-	-	-	-	$\frac{\text{CO}_2}{\text{O}_2} = 3.28$
28.2	-	-	-	-	-	1.01
33.8	-	-	-	-	-	1.18
38.8	-	-	-	-	-	0.91

VON FREY and GRUBER² showed that in a dog's muscle, with artificial circulation, contractions are accompanied by an increase in the carbon dioxid added to the blood, but they found this increase variable (46-10 per cent.) and *less than the corresponding absorption of oxygen*, so that the respiratory ratio became lowered during contraction. TISSOT³ showed that the production of carbon dioxid in

¹ Versuche über den Einfluss der Temperatur auf die Respiration des ruhend's Muskels. DuBois-Reym. Archiv für Physiol. 1885:38-66.

² Versuche über den Stoffwechsel des Muskels. DuBois-Reym. Archiv für Physiol. 1885:533-562.

³ Recherches sur la respiration musculaire. Arch. de Phys. Norm. et Path. V. 6:838-844. Also, Variation des échanges gazeux d'un muscle extrait du corps. *Op. et ser. cit.* 7:641-653. 1895.

excised muscles was increased if the muscles were killed by heat or were fatigued by prolonged stimulation. The output of carbon dioxid in such cases *was not related to the rate of absorption of oxygen*. Six years ago FLETCHER,⁴ using Blackman's apparatus, the most intricate and accurate apparatus yet devised for following gaseous exchanges, showed that the evolution of carbon dioxid from excised frog's muscles is *independent of the amount of oxygen taken up during the period*. He distinguished in the production of carbon dioxid, first, a short period (about six hours), which he thinks dependent upon the presence of oxygen; and second, a long-continued evolution of carbon dioxid "due to chemical processes occurring spontaneously within the muscle, in which complex molecules are replaced by simpler ones, with the conspicuous results of the appearance of [sarcolactic] acid and of free carbon dioxid." He adds: "Under suitable conditions the occurrence of active contractions in an excised muscle is *not* accompanied by an increase in the rate at which carbon dioxid is yielded by the muscle," though oxygen is abundantly supplied then by the blood. He does find, however, an increased formation of other decomposition products.

CHAUVEAU and KAUFMANN, as long ago as 1887, found that the output of carbon dioxid from the levator muscle of a horse's upper lip was greater during activity than during rest, and *contained more oxygen than that absorbed in same time*.⁵

A great number of researches of the same tenor can be found in botanical literature. A single example must suffice. In an elaborate paper PURJEWICZ shows⁶ that the variations in the carbon dioxid produced and the oxygen absorbed during a given period under various conditions *are not parallel*, the amount of carbon dioxid ranging within far wider limits than the oxygen. Thus, the carbon dioxid varied from —14 to 120 per cent. of the average; the oxygen varied from 0 to 48 per cent. of the average. PURJEWICZ, indeed, expresses his conviction that the respiratory ratio has no value as indicating the actual course of respiration, and would separate

⁴ Survival respiration of muscle. Jour. Physiol. 23:10-99. 1898.

⁵ Le coefficient de l'activité nutritive et respiratoire des muscles. Compt. Rend. Acad. Sci. France 104:1126-1132. 1887.

⁶ Physiol. Unters. über Pflanzenatmung. Jahrb. Wiss. Bot. 35:573-610. 1900.

the taking up of oxygen and the production of carbon dioxide as two processes, only indirectly related.

It is clear that such results as have been cited became difficult to reconcile with the idea that respiration is combustion, and so an attempt was made to evade the force of the facts, while maintaining the comparison, by introducing a qualifying term and speaking of respiration as "physiological combustion." This modification, however, blinks the difficulty; it does not remove it.

Before passing from this part of my subject I may mention another false conception, which is more or less directly dependent on the notion that respiration is combustion. One often finds respiration described as a gaseous exchange—the taking up of oxygen and giving off of carbon dioxide—a trade between the atmosphere and the body. Clearly this is another case of transferring the superficial interpretation of our own physiological processes to other organisms. The exchange that takes place between the tissues and the blood, between the blood and air in the lungs, gives the foundation, and the unessential phenomena of respiration become substituted for the essential. It would be quite as correct to describe photosynthesis as "an exchange of gases," for carbon dioxide is taken up and oxygen is eliminated. Yet no one ever thinks so superficially of this process.

ANAEROBIC RESPIRATION.

For three quarters of the last century it was supposed that the evolution of carbon dioxide could only occur when free oxygen was available. But in the early seventies PFLÜGER discovered what seemed a peculiar form of respiration. He found that a frog put into a vacuum continued to give off carbon dioxide; and presently the same phenomenon was observed by PFEFFER and others in plants. So firmly had the conception of combustion fastened itself upon physiologists, that when this anaerobic respiration came to be explained, it was supposed that certain molecules of organic matter within the cell gave up their oxygen to others, that they might thus be burned in the body-furnace to yield energy. Hence arose the term "intramolecular respiration."

The study of anaerobic respiration, misleading as this early interpretation of it was, has thrown in late years a very great light

upon normal or aerobic respiration. Here is a process which results in the evolution of energy, and gives rise to one important end-product of aerobic respiration, viz., carbon dioxid; yet it early became evident that it could not be counted a process of combustion, at least in any sense in which combustion was then understood. Plainly, the changes that were going on within the organism, which enabled it to give off carbon dioxid when no free oxygen was to be had, could only be a rearrangement of atomic groups within the molecule and the formation of products which were simpler than those from which they arose.

FERMENTATION.

The process of fermentation, first thoroughly explored by PASTEUR, whose results have been much extended by the brilliant researches of HANSEN and many others, are evidently related to those of respiration by the nature of the end products and the conditions under which the processes occur. Indeed, when one compares the end products of respiration and of alcoholic fermentation he finds them to be identical in all respects. Other sorts of fermentation likewise yield many substances that are found originating in the metabolism of the higher plants.

We have, then, three modes of energy-release, which are evidently closely related, if not identical; aerobic respiration, anaerobic respiration, and fermentation. Their relations, so far as was known in 1898, were stated by PFEFFER in his *Pflanzenphysiologie* and need not be reviewed.

THE COURSE OF RESPIRATION.

In translating that work (p. 519) EWART wrote: "The actual course of respiration within the protoplast is quite obscure." PFEFFER himself says (p. 551): "Our knowledge of the inherent protoplasmic mechanism is too incomplete to afford a sound basis for any theory concerning the phenomena of respiration." Fortunately, knowledge in the last six years has broadened, and I believe that it is possible now to see pretty clearly what the actual course of respiration is. Perhaps you will say, to foresee rather than to see—but hypothesis must outrun demonstration. The advances to which we are indebted for deeper insight are in three fields: first, the chemistry of pro-

teids; second, the course of combustion, especially at low temperatures; third, the nature of anaerobic respiration, and its relation to aerobic respiration. Let me speak of these in order.

CHEMISTRY OF THE PROTEIDS.

A knowledge of the proteids, complex as they are, could be obtained only by a study of their decomposition products. Now there is a very remarkable uniformity in these decomposition products. No matter what the organism from which they are derived, no matter how simple they are or how complex, when broken up by the process of digestion, or by boiling with acids, they yield invariably a series of products which have become in the last few years much better known. These are amino- or amido-acids; such substances as leucin, tyrosin, arginin, glutamin, glycocoll, etc. Materials of this kind are invariably present, and certain ones are so invariably present that they can be used as the basis of distinctive tests for the occurrence of digestion or similar decompositions of proteids. This gave a clue to the nature of proteids which was followed by several observers, notably by KOSSEL, in the study of what are believed to be the very simplest proteids, because of the fewness and uniformity of the fractions into which they break up. These are the protamines. It has become clear from the study of these simple proteids that they are made up in somewhat the same way as the polysaccharides among the carbohydrates, that is by linking together a series of the amido-acids. This is possible because the amido-acids have a peculiar construction. They are, so to speak, different on different sides. On one side is an acid group and on the other a basic group; and so the amido-acids can hang together in chains, or even be condensed or polymerized to make a simple proteid. Among the amido-acids, as in the carbohydrates, there are certain atomic groups, like CH_3 , CH_2 , CHOH , CH_2OH , COOH , etc., which recur again and again, and in such groups the possibility of replacing a hydrogen atom or a hydroxyl radicle by some other atomic group is very great.

Note, for instance, the comparatively simple acetic acid, $\text{CH}_3 \cdot \text{COOH}$. If we replace one of the three H atoms by the amido group, NH_2 , we have at once an amido-acid, glycocoll, $\text{CH}_2(\text{NH}_2) \cdot \text{COOH}$,

which is one of the sorts of material out of which proteids can be made. Out of an alcohol or out of a sugar we get just the groups CHOH , CH_2OH , etc., from which these amido-acids may be constructed when nitrogenous substances are present to supply the amido group NH_2 . Thus the mode of construction of the proteids has been found to show a likeness to that of the complex carbohydrates, and it has long been known that the carbon groups were very much alike in both. It further appears that when the proteids are digested by any organism they break down into these fragments, of one sort and another, the amido-acids, the amides, etc., which may be put together again in new form to constitute the peculiar proteids of that particular organism. We may thus get one proteid out of any other by the breaking up of the complex molecule and the rearrangement of its constituent fragments. This fragmentation is readily accomplished by the proteolytic enzymes, which probably act on these bodies as the diastases do on carbohydrates.

OXIDATION.

The second important line of progress has been in the study of the oxidation of carbon compounds at low temperatures. For our purpose the important facts, which have only recently been developed, are that the oxygen of the air does not combine directly with carbon or with carbon monoxid to form CO_2 , or with hydrogen to form H_2O , as has heretofore been supposed.

As long ago as 1893 DIXON'S researches⁷ on explosive gases showed that molecular oxygen was by far the most effective of the atmospheric gases in *retarding* combustion. This surprising result could not be interpreted then, and only in the light of TRAUBE'S theory and the studies of BONE and others⁸ on the oxidation of gases like methane and ethane at low temperatures, has it been possible to picture the mechanism of such combustion. This has been done by ARMSTRONG,⁹ who holds (with TRAUBE) that the substances do

⁷ The rate of explosion in gases. Phil. Trans. Roy. Soc. London A. **184**:97-188. 1893.

⁸ BONE and WHEELER: The slow oxidation of methane. Trans. Chem. Soc. London **81**:535-545. 1902; **84**:1074-1087. 1903.

BONE and STOCKINGS: Slow combustion of ethane. Trans. Chem. Soc. London **85**:693-727. 1904.

⁹ Retardation of combustion by oxygen. Chem. News **90**:25. 1904. Mechanism of combustion. Trans. Chem. Soc. London **83**:1088. 1903.

not undergo direct oxidation but hydroxylation, *i. e.*, its hydrogen atoms are successively replaced by hydroxyl radicles, with consequent splitting into various intermediate products, such as carbon monoxid and hydrogen peroxid, carbonic acid and water being the end products. ARMSTRONG says:

There is little reason to suppose that changes take place at high temperatures in rapid combustions in ways very different from those in which they occur at lower temperatures. . . . The effective operation is not the mere blow due to impact or the vibration caused by this in the molecule, but the conjunction of compatible molecules and the consequent formation of composite systems within which change can occur. In so far as temperature influences the formation of compatible systems, either as regards their character or the rate at which they arise, temperature has an influence, but probably not otherwise.

I ask you to notice, then, that the process of combustion is now being interpreted in the light of changes like those which have long been known in organisms under the name of hydrolysis, and are the characteristic mode of action of enzymes. Thus, when starch is acted upon by diastase it is probably by repeated reactions between water, dissociated into hydrogen and hydroxyl groups, and oxygen—in other words, by continued hydroxylation—that it becomes ready to fall apart into a series of dextrines and finally into maltose. Diastase in some way facilitates this dissociation. Maltase takes up the task, and maltose, further hydroxylized, cleaves into two molecules of glucose. Then zymase may lend its aid and hydrolyze the glucose molecule into lactic acid, breaking the latter still further into carbon dioxid and alcohol.

The mechanism of the digestion of starch is not known in detail, though the various intermediate products have been fairly well studied. The usual assumption made is merely that water combines with the starch under the action of diastase. I have carried the theory a little further into detail, as seems warranted by the studies of combustion. It is worthy of note also that the late steps in the process, the hydrolysis of glucose by zymase, have been designated by the term “fermentation.” The combustion of starch has likewise not been examined, but as the end products are identical with those of digestion, it is not at all improbable that the intermediate steps are the same, though they succeed one another too fast to be followed by means at present available.

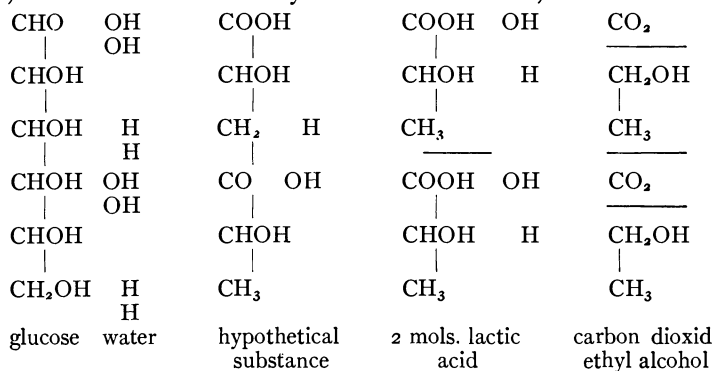
I need hardly remind you that our present ideas of the dynamics

of chemical reactions forbid us to believe that such dissociation does not go on slightly at low temperatures, even when unaided. But it is so slow as to be ordinarily beyond our measurement. The enzymes seem to be mere accelerators of the several processes, perhaps preparing "compatible systems," as high temperature may do in combustion; perhaps entering into union with the substance they act on and forming compounds which are dissociable at ordinary temperatures in appreciable amounts.

The clue to an understanding of respiration has been found, therefore, not by comparing it to combustion, which was so long misleading, but by assimilating combustion to respiration. We may hope that chemists will restrict the term "combustion" or introduce a new one that will make more obvious the mode of action. Physiologists at least will do well to drop "combustion" altogether from their vocabulary, as neither the past conception of it nor its probable use in the future conduces to clearness of thought.

NATURE OF ANAEROBIC RESPIRATION.

The third line of advance has been in a study of the relations of fermentation and anaerobic respiration. The first step was that long-sought discovery by BUCHNER, that the process of fermentation by yeast is brought about by the action of an enzyme which breaks up certain hexose sugars into carbon dioxid and alcohol. But a further step in advance has lately been taken. It appears from the work of BUCHNER and MEISENHEIMER¹⁰ that the alcoholic fermentation is not direct, but that it occurs always in indirect fashion, as shown below:



¹⁰ Die chemischen Vorgänge bei alkoholischen Gärung. Ber. Deutsch. Chem. Gesells. 37:419-428. 1904.

STĚPANĚK has reached the same conclusion,¹¹ and MAZĚ¹² has found acetic acid as an intermediate product in alcoholic fermentation by a different yeast. The interest of the discovery that inactive ethylidene lactic acid is the intermediate substance in this process of fermentation lies in the fact that one of the two acids of which that is composed namely, *d*-ethylidene lactic acid, or sarcolactic acid, is formed as a product of respiration when proteids break down in the working, fatigued, or dying muscle. FLETCHER observed this as a more prominent product of contracting muscles than carbon dioxid itself. Thus a regular product of fermentation is also formed in the ordinary course of respiration.

The analogy between anaerobic respiration and fermentation had been suggested early—even by PASTEUR—and has thus been growing closer with each added bit of knowledge. But the precise way in which the destruction of the living substance went on in anaerobic respiration was still unknown. Fermentation had been shown to be due to an enzyme. Was anaerobic respiration also due to an enzyme?

Of course, enzymes are known to be present in a great many of the parts of plants, and the oxidizing enzymes seemed to be the sort to be sought. But none seemed to answer the conditions. At last, however, the object appears to have been attained. STOKLASA, in a series of papers published in various journals,¹³ but all dealing with the same general problem, declares he has found in various tissues of animals, and in considerable number of plants, an enzyme analo-

¹¹ Ueber die aerobe und anaerobe Atmung der Eier. *Centralbl. Physiol.* **18**: 188–205. 1904.

¹² Utilization du carbone ternaire. *Ann. Inst. Pasteur* **18**: 277–303. 1904.

¹³ STOKLASA: Identität anaerob. Atmung u. Gärung. *Oesterr. Chem. Zeit.* 1903. (Not seen.)

STOKLASA, JELINEK, and VITEK: Der anaer. Stoffwechsel der höh. Pfl. und seine Beziehung z. alcoh. Gärung. *Beitr. z. Chem. Physiol. u. Path.* **3**: 460. 1903.

STOKLASA and ČERNÝ: Isolierung des die anaer. Atmung der Zelle der höh. org. Pfl. und Tiere bewirk. Enzymes. *Ber. Deutsch. Chem. Gesells.* **36**: 622–634. 1903.

—: Ueber die anaer. Atm. der Tierorgane u. über die Isolierung eines gärungs-erregenden Enzymes aus dem Tierorganismus. *Zentralbl. Physiol.* **16**: 652–658. 1903.

STOKLASA: Ueber die Atmungsenzyme. *Ber. Deutsch. Bot. Gesells.* **22**: 358–361. 1904.

gous to BUCHNER's zymase, and like it glycolytic. This enzyme he reports in leaves and roots of beet, tubers of potato, seeds, seedlings, and young plants of pea, seedlings of barley, and entire plants of *Paris quadrifolia*. Confirmatory results have (naturally enough) been obtained by several students or assistants who have evidently been engaged upon portions of the problem under the guidance of STOKLASA. It is only fair to say that MAZÉ has strongly criticised STOKLASA's methods from the bacteriological side, and declares himself unable to secure like fermentation under aseptic conditions;¹⁴ though STOKLASA claims to have guarded carefully against infection and to have rejected contaminated cultures. Independently, MAZÉ has found what he calls zymase, in connection with pea seedlings, *Aspergillus* and *Eurotiopsis*. He declares it "an enzyme normal to all plants, arising like all other enzymes during vegetative (aerobic) life." In the higher plants, however, and in most fungi it "is oxidized with the greatest ease, so that one never finds more than a trace of it."

MAZÉ and STOKLASA interpret their results somewhat differently, MAZÉ holding the process of fermentation to be a nutritive one,¹⁵ sugar being only assimilable when fermented and the nascent alcohol thus made available, while STOKLASA believes fermentation to be merely anaerobic respiration and essentially a process for the immediate release of energy.

Confirmation comes also from another source, for GODLEWSKI,¹⁶ working with lupines, finds similar products, and concludes that their "anaerobic respiration is identical with alcoholic fermentation, of at least in essence dependent on it."

Moreover, KOSTYTSCHEW¹⁷ and MAXIMOW¹⁸ have found in *Aspergillus* an enzyme which is analogous to zymase and is responsible

¹⁴ Various papers in *Annales Inst. Pasteur* 18: 1904.

¹⁵ IWANOWSKY in 1894 propounded the theory that alcoholic fermentation is a pathological case in the nutrition of yeast, called forth by the abnormal composition of the nutritive medium.

¹⁶ Weiterer Beitr. z. Kennt. der intramol. Atmung. *Bull. Acad. Sci. Cracovie* 1904:115-158. See also his earlier paper with POLZENIUSZ. *Bull. cit.* April 1901.

¹⁷ Ueber Atmungsenzyme der Schimmelpilze. *Ber. Deutsch. Bot. Gesells.* 22: 207-215. 1904.

¹⁸ Zur Frage über die Atmung. *Ber. Deutsch. Bot. Gesells.* 22:225-235. 1904.

for the formation of CO_2 whether in aerobic or anaerobic respiration.

Thus several independent observers are testifying to the rather widespread occurrence of an enzyme which brings about a disruption of plant substance, under most varied external conditions, whether the plant be fed on one food or another,¹⁹ this dissociation resulting in the formation of carbon dioxide and of various other products.

THE MECHANISM OF RESPIRATION.

Let us now focus the light coming from the chemistry of proteids, the mechanism of combustion, and the physiology of respiration, to form a picture of what goes on in the body.

First: We should conceive of the respiratory dissociation as taking place in the living material of the body and not in a food still unassimilated. Experiments with a wide range of foods have shown that they affect the intake of oxygen and the output of carbon dioxide in the most diverse ways, whence it has been assumed that the respiratory ratio varies because of the way in which the given food is oxidized. I do not say that it is not possible for the protoplasm to decompose a sugar directly or to oxidize a fat. But it must be remembered that in no case has it been experimentally proved that the food *is* directly attacked, and that all the facts can be explained on the other assumption, and some of them very much better than on the theory of direct oxidation. Moreover, the lability of proteids which have been raised to the life-level is their most striking characteristic as contrasted with their ordinary stability.

In such labile material the *second* step is easily conceivable. There occurs a shifting of the atomic groups within the molecule, perhaps as a result of the last step in their anabolism—the addition of hydroxyl groups from the water everywhere present. Dissociation follows necessarily; very slow perhaps at ordinary temperatures and with a scanty supply of water, yet sufficient evidently for the maintenance of life. Such conditions may very well be those obtaining in resting organs, spores, and seeds. But normally this cleavage may go on at a measurable rate, without anything more than the

¹⁹ See a paper by KOSZYTSCHÉW which has just come to hand (Ueber die normale und die anaerobe Atmung bei Abwesenheit von Zucker. Jahrb. Wiss. Bot. 40:563-592. 1904), showing the erroneousness of DIAKONOW's idea that anaerobic respiration is only possible when sugar is supplied.

inevitable dissociation when hydroxylation has progressed to a certain point. It seems, however, that there is generally—perhaps always—a hastening of this process, and that the highly unstable protoplasm is dissociated so rapidly that it liberates not only the energy immediately utilized in growth, movement, etc., but also an excess sufficient to be easily measured by so coarse an instrument as the thermometer. Catalytic agents like the enzymes are certainly (I think I may be permitted so strong an assertion) the usual accelerators. And it is highly probable that an enzyme identical with zymase or at least analogous to it, is an active though secondary agent in this acceleration. It may very well be also that those changes outside the protoplast (whether without the organism or not) that are called stimuli accelerate still further the katabolism, even to an explosive speed in some cases.

This primary dissociation may plainly be independent of free oxygen, though it is hardly conceivable that there will not be some oxygen present unless the plant has grown under most unusual conditions, which one can scarcely realize experimentally. The products of this decomposition are not sufficiently known, nor is their precise character important for our discussion. Among them are certainly the more complex amido-acids, carbon dioxide, and alcohol.

Third: Up to this point the respiratory processes are quite alike whether the plants grow in the air or apart from it. If sufficient oxygen be not present, the disruptive processes may reach an equilibrium, just as an electrolyte practically ceases to pass a current of electricity unless a depolarizer be present. So in the hydroxylation of proteids, there is needed some substance to disturb constantly, in one direction or another, the equilibrium that tends to be reached. The common agent in this is oxygen. Of course, oxygen can hardly be the only depolarizer that can promote further action. Thus, MAZÉ found the presence of levulose conduced to the continued evolution of carbon dioxide in the absence of oxygen, and it is quite possible that levulose took up the rôle of depolarizer, though MAZÉ does not so interpret his observation.

In anaerobic respiration insufficient oxygen is supplied. Its products that have been most observed, and are therefore (though doubtless groundlessly) counted its characteristic products, are carbon

dioxid and alcohol. Indeed, lactic seems an equally characteristic though transient product. The fact that hydrogen has also been often recognized among them supports the interpretation of the function of oxygen just suggested, and accords thoroughly with the theory of hydroxylation. In that process hydrogen atoms from the dissociation of water would be left free in case there was insufficient oxygen to form H_2O_2 .

Fourth: But if the organism can get an adequate supply of oxygen, the katabolism continues, some of the most complex previous products breaking up by hydroxylation and thermal cleavage. Among the fragments are undoubtedly some that lose in part those very groups in which sugars, alcohols, fatty acids, etc., are peculiarly rich. These are rebuilt at the expense of such foods, which therefore disappear as a result of respiration. That ethyl alcohol does not persist when oxygen is present may mean either that it is decomposed, or that in its nascent state it is assimilated in the rebuilding of proteids, for we have seen how easily acetic acid, one of its oxidation products, can be converted into an amido-acid, glycocoll, and be thus in direct line for reconstructive metabolism.

This, in its fundamental features, is the theory I have presented in lectures to advanced classes since 1898, though always as more or less a speculation. For various details I am indebted to the recent literature, already cited. Because it is capable of explaining the observed facts, which are now sufficiently numerous to demand a coherent explanation, I conceive it to be entitled to the dignity of a theory. Time forbids the discussion of details, and many points have been considered that cannot be here presented.

This theory maintains the direct relation of aerobic and anaerobic respiration, whose genetic connection was long since advocated by PFEFFER. Anaerobic respiration is the primary process in all organisms. Whether aerobic respiration occurs or not depends upon the availability of oxygen. The relation of fermentation to the process is not wholly clear; for although fermentation gives rise to the same products as anaerobic respiration, this may depend in part upon respiratory decompositions, such as have been described, and in part upon digestion, which, as IWANOWSKY and MAZÉ think, render the alcohol from sugars available for assimilation. I am inclined to

believe that in fermentation we deal with an exaggerated anaerobic respiration, the active ferments being plants in which zymase is produced in such amounts that it can attack sugars outside the organism, and thus secure sufficient energy with a minimum destruction of the protoplasm.

ENERGESIS.

Finally, I may suggest that for didactic purposes it is desirable to have a word other than "respiration" to designate the disruptive processes by which energy is released, leaving "respiration" to designate the more superficial phenomena of aeration with which plant physiologists are but little concerned. Perhaps the word "respiration" is already too firmly imbedded in literature to be so limited. It will at least do no harm to propose that the terms "aerobic and anaerobic *energesis*" be considered, to which "fermentative *energesis*" may be added if necessary.

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